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         AUG 27 CAS definition of basic patents expanded to ensure
                 comprehensive access to substance and sequence
                 information
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                 to be discontinued
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                 exemplified prophetic substances
                 WPIDS, WPINDEX, and WPIX coverage of Chinese and
NEWS 13
         SEP 26
                 and Korean patents enhanced
NEWS 14
         SEP 29
                IFICLS enhanced with new super search field
NEWS 15
         SEP 29 EMBASE and EMBAL enhanced with new search and
                 display fields
NEWS 16
         SEP 30 CAS patent coverage enhanced to include exemplified
                 prophetic substances identified in new Japanese-
                 language patents
NEWS 17 OCT 07
                 EPFULL enhanced with full implementation of EPC2000
NEWS 18 OCT 07 Multiple databases enhanced for more flexible patent
                 number searching
NEWS 19 OCT 22 Current-awareness alert (SDI) setup and editing
                 enhanced
NEWS 20
         OCT 22
                 WPIDS, WPINDEX, and WPIX enhanced with Canadian PCT
                 Applications
NEWS 21
                 CHEMLIST enhanced with intermediate list of
         OCT 24
                 pre-registered REACH substances
NEWS 22 NOV 21 CAS patent coverage to include exemplified prophetic
                 substances identified in English-, French-, German-,
                 and Japanese-language basic patents from 2004-present
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        112475 DEGREES
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         11183 SULFATION
            43 SULFATIONS
         11196 SULFATION
                (SULFATION OR SULFATIONS)
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            11 L3 AND DEGREE AND SULFATION
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    ANSWER 1 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
T. 4
ACCESSION NUMBER:
                         2008:452050 CAPLUS
DOCUMENT NUMBER:
                         149:561
TITLE:
                         Sulfated K5 Escherichia coli polysaccharide
                         derivatives as wide-range inhibitors of genital types
                         of human papillomavirus
AUTHOR(S):
                         Lembo, David; Donalisio, Manuela; Rusnati, Marco;
                         Bugatti, Antonella; Cornaglia, Maura; Cappello, Paola;
                         Giovarelli, Mirella; Oreste, Pasqua;
                         Landolfo, Santo
                         Department of Clinical and Biological Sciences, San
CORPORATE SOURCE:
                         Luigi Gonzaga Hospital, University of Turin, Turin,
                         10043, Italy
SOURCE:
                         Antimicrobial Agents and Chemotherapy (2008), 52(4),
                         1374-1381
                         CODEN: AMACCQ; ISSN: 0066-4804
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American Society for Microbiology

PUBLISHER:

DOCUMENT TYPE: Journal LANGUAGE: English

Genital human papillomaviruses (HPV) represent the most common sexually transmitted agents and are classified into low or high risk by their propensity to cause genital warts or cervical cancer, resp. Topical microbicides against HPV may be a useful adjunct to the newly licensed HPV vaccine. A main objective in the development of novel microbicides is to block HPV entry into epithelial cells through cell surface heparan sulfate proteoglycans. In this study, selective chemical modification of the Escherichia coli K5 capsular polysaccharide was integrated with innovative biochem. and biol. assays to prepare a collection of sulfated K5 derivs. with a backbone structure resembling the heparin/heparan biosynthetic precursor and to test them for their anti-HPV activity. Surface plasmon resonance assays revealed that O-sulfated K5 with a high degree of sulfation [K5-OS(H)] and N,O-sulfated K5 with a high [K5-N,OS(H)] or low [K5-N,OS(L)] sulfation degree, but not unmodified K5, N-sulfated K5, and O-sulfated K5 with low levels of sulfation, prevented the interaction between HPV-16 pseudovirions and immobilized heparin. In cell-based assays, K5-OS(H), K5-N,OS(H), and K5-N,OS(L) inhibited HPV-16, HPV-18, and HPV-6 pseudovirion infection. Their 50% inhibitory concentration was between 0.1 and 0.9 $\mu g/mL$, without evidence of cytotoxicity. These findings provide insights into the design of novel, safe, and broad-spectrum microbicides against genital HPV infections.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AU Lembo, David; Donalisio, Manuela; Rusnati, Marco; Bugatti, Antonella; Cornaglia, Maura; Cappello, Paola; Giovarelli, Mirella; Oreste, Pasqua; Landolfo, Santo

AB . . . precursor and to test them for their anti-HPV activity. Surface plasmon resonance assays revealed that O-sulfated K5 with a high degree of sulfation [K5-OS(H)] and N,O-sulfated K5 with a high [K5-N,OS(H)] or low [K5-N,OS(L)] sulfation degree, but not unmodified K5, N-sulfated K5, and O-sulfated K5 with low levels of sulfation, prevented the interaction between HPV-16 pseudovirions and immobilized heparin. In cell-based assays, K5-OS(H), K5-N,OS(H), and K5-N,OS(L) inhibited HPV-16, HPV-18, and . .

TT 78245-16-6D, repeating unit of 78245-16-6D, repeating unit of, N-sulfated derivs. 78245-16-6D, repeating unit of, high degree of N,O-sulfated derivs. 78245-16-6D, repeating unit of, high degree of O-sulfated derivs. 78245-16-6D, repeating unit of, low degree of N,O-sulfated derivs. 78245-16-6D, repeating unit of, low degree of O-sulfated derivs.

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(sulfated K5 escherichia coli polysaccharide derivs. as widerange inhibitors of genital types of human papillomavirus)

L4 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:486971 CAPLUS

DOCUMENT NUMBER: 141:87601

TITLE: Chemically sulfated Escherichia coli K5 polysaccharide

derivatives as extracellular HIV-1 Tat protein

antagonists

AUTHOR(S): Urbinati, Chiara; Bugatti, Antonella; Oreste,

Pasqua; Zoppetti, Giorgio;

Waltenberger, Johannes; Mitola, Stefania; Ribatti,

Domenico; Presta, Marco; Rusnati, Marco

CORPORATE SOURCE: Unit of General Pathology and Immunology, Department

of Biomedical Sciences and Biotechnology, School of

Medicine, University of Brescia, Brescia, 25123, Italy

SOURCE: FEBS Letters (2004), 568(1-3), 171-177

CODEN: FEBLAL; ISSN: 0014-5793

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal LANGUAGE: English

AB The HIV-1 transactivating factor (Tat) acts as an extracellular cytokine on target cells, including endothelium. Here, we report about the

Tat-antagonist capacity of chemical sulfated derivs. of the Escherichia coli

K5 polysaccharide. O-sulfated K5 with high sulfation

degree (K5-OS(H)) and N,O-sulfated K5 with high (K5-N,OS(H)) or

low (K5-N,OS(L)) <u>sulfation</u> <u>degree</u>, but not unmodified K5, N-sulfated K5, and O-sulfated K5 with low <u>sulfation</u>

degree, bind to Tat preventing its interaction with cell surface heparan sulfate proteoglycans, cell internalization, and consequent HIV-LTR-transactivation. Also, K5-OS(H) and K5-N,OS(H) prevent the interaction of Tat to the vascular endothelial growth factor receptor-2 on endothelial cell (EC) surface. Finally, K5-OS(H) inhibits $\alpha v \beta 3$

endothelial cell (EC) surface. Finally, K5-OS(H) inhibits $\alpha v\beta 3$ integrin/Tat interaction and EC adhesion to immobilized Tat.

Consequently, K5-OS(H) and K5-N,OS(H) inhibit the angiogenic activity of Tat in vivo. In conclusion, K5 derivs. with distinct sulfation

patterns bind extracellular Tat and modulate its interaction with cell surface receptors and affect its biol. activities. These findings provide the basis for the design of novel extracellular Tat antagonists with possible implications in anti-AIDS therapies.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AU Urbinati, Chiara; Bugatti, Antonella; Oreste, Pasqua;
Zoppetti, Giorgio; Waltenberger, Johannes; Mitola, Stefania;
Ribatti, Domenico; Presta, Marco; Rusnati, Marco

AB . . . we report about the Tat-antagonist capacity of chemical sulfated derivs. of the Escherichia coli K5 polysaccharide. O-sulfated K5 with high sulfation degree (K5-OS(H)) and N,O-sulfated K5 with high (K5-N,OS(H)) or low (K5-N,OS(L)) sulfation degree, but not unmodified K5, N-sulfated K5, and O-sulfated K5 with low sulfation degree, bind to Tat preventing its interaction with cell surface heparan sulfate proteoglycans, cell internalization, and consequent HIV-LTR-transactivation. Also, K5-OS(H) and . . immobilized Tat. Consequently, K5-OS(H) and K5-N,OS(H) inhibit the angiogenic activity of Tat in vivo. In conclusion, K5 derivs. with distinct sulfation patterns bind extracellular Tat and modulate its interaction with cell surface receptors and affect its biol. activities. These findings provide. . .

L4 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:1007021 CAPLUS

DOCUMENT NUMBER: 140:47543

TITLE: Low-molecular weight oversulfated polysaccharide

INVENTOR(S): Oreste, Pasqua Anna; Zoppetti,

Giorgio

PATENT ASSIGNEE(S): Italy

SOURCE: PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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                                           IT 2002-MI1345
                                                              A 20020618
PRIORITY APPLN. INFO.:
                                                               A 20020618
                                            IT 2002-MI1346
                                            IT 2002-MI1854
                                                               A 20020827
                                            WO 2003-IB2347
                                                               W 20030617
AΒ
     Low-mol. weight (LMW) K5-N, O-oversulfates are described, having a
     sulfation degree of 3.2 to 4 and a mean mol. weight of
     about 3000 to about 6000, obtainable by depolymn. of corresponding
     K5-N,O-oversulfates or starting from LMW-K5-N-sulfates by O-oversulfation
     of a tertiary amine or quaternary ammonium salt thereof and subsequent
     N-resulfation of the K5-amine-O-oversulfate thus obtained. Furthermore,
     pharmaceutical compns. containing these LMW-K5-N, O-oversulfates having
     antiangiogenic and antiviral, in particular anti-HIV-1 activity are
     described. Intermediate LMW-K5-N-sulfates are also described.
REFERENCE COUNT:
                               THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
                              RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
     Oreste, Pasqua Anna; Zoppetti, Giorgio
ΙN
AΒ
     Low-mol. weight (LMW) K5-N, O-oversulfates are described, having a
     sulfation degree of 3.2 to 4 and a mean mol. weight of
     about 3000 to about 6000, obtainable by depolymn. of corresponding. .
     Angiogenesis inhibitors
ΙT
     Anti-AIDS agents
     Antiviral agents
     Deacetylation
     Depolymerization
     Drug delivery systems
     Human
     Reduction
       Sulfation
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(preparation of low-mol. weight oversulfated polysaccharide having

antiangiogenic and antiviral activities)

L4 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:1007020 CAPLUS

DOCUMENT NUMBER: 140:47542

TITLE: Process for the manufacture of

N-acyl-(epi)K5-amine-o-sulfate derivatives and

products thus obtained

INVENTOR(S): Oreste, Pasqua Anna; Zoppetti,

Giorgio

PATENT ASSIGNEE(S): Italy

SOURCE: PCT Int. Appl., 74 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

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CN	1675	249			Α						2003-					0030	617	
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AB A method is described for the oversulfation of (epi)KS-N-sulfates to obtain (epi)K5-amine-O-oversulfates at extremely high degree of sulfation and for the transformation of these intermediates into new N-acyl-(epi)K5-amine-O-oversulfates basically free of activity on the coagulation parameters and useful in the cosmetic or pharmaceutical field. Also described are pharmaceutical compns. containing, as one of their active ingredients, an (epi)K5-amine-O-oversulfate.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IN Oreste, Pasqua Anna; Zoppetti, Giorgio

AB A method is described for the oversulfation of (epi)KS-N-sulfates to obtain (epi)K5-amine-O-oversulfates at extremely high degree of sulfation and for the transformation of these intermediates into new N-acyl-(epi)K5-amine-O-oversulfates basically free of activity on the coagulation parameters and useful. . .

IT Acylation

Cosmetics

Depolymerization

Diastereomers

Drug delivery systems

Epimerization

Sulfation

(manufacturing of acyl-(epi)K5-amine sulfate derivs. for cosmetics and pharmaceuticals)

L4 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:1007019 CAPLUS

DOCUMENT NUMBER: 140:47541

TITLE: Epimerized derivatives of K5 polysaccharide with a

very high $\underline{\text{degree}}$ of $\underline{\text{sulfation}}$

INVENTOR(S): Oreste, Pasqua Anna; Zoppetti,

Giorgio

PATENT ASSIGNEE(S): Italy

SOURCE: PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

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	US 20060014718	A1	20060119		2005-518302	20050531
PRIC	RITY APPLN. INFO.:				2002-MI1345	A 20020618
					2002-MI1346	A 20020618
					2002-MI1854	A 20020827
					2003-IB2338	W 20030617
AB	A method is describe	ed for	the oversul	fati	on of epiK5-N-su	lfate to obtain
	an epiK5-amine-0-ove	ersulfa	ate with ver	y hi	gh sulfation	
	degree which, by sub	sequer	nt N-sulfati	on,	provides new	
	epiK5-N,O-oversulfat	e-der:	ivs. with a	sulf	ation degree	
	of at least 4, basic	cally f	free of acti	vity	on the coagulat	ion parameters
	and useful in the co					
	new low mol. weight	epiK5-	-N-sulfates	usef	ul as intermedia	ates in the
prep	aration of					
	the corresponding LM	_				
REFE	RENCE COUNT:	9				AILABLE FOR THIS
						IN THE RE FORMAT
ΤΙ	Epimerized derivativ	res of	K5 polysacc	hari	de with a very h	nigh
	degree of sulfation	_				
IN	Oreste, Pasqua Anna;				C 'TZE N	3.5
AB	A method is describe					iliate to obtain
	an epiK5-amine-0-ove					
	degree which, by sub epiK5-N,O-oversulfat					
	of at least 4, basic					ion parameters
	and useful in the co	_		_	-	=
ST	polysaccharide prepr					•
01	cosmetic pharmaceut:		zrichia cpin	CIIZ	acion <u>sallacion</u>	
ΙT	Cosmetics	LCGI				
	Deacetylation					
	Depolymerization					
	Diastereomers					
	Drug delivery system	ns				
	Epimerization					
	Escherichia coli					
	Sulfation					
	(preparation, ep					accharide of
	Escherichia coli			gree	of <u>sulfation</u>	
	for cosmetics or					
ΙT	Polysaccharides, pre	eparat:	ion			
	Uronic acids			. О. П. <i>(</i>	D	(D) 1 1 1
	RL: BPN (Biosynthet:					(Blological
	study); PREP (Prepar (preparation, ep				_	acharida of
	Escherichia coli					accharide of
	for cosmetics or			gree	or <u>surration</u>	
ΙT	Polysaccharides, bio					
	RL: COS (Cosmetic us			es):	SPN (Synthetic	preparation): THII
	(Therapeutic use); H					
	(Uses)	7101 (1	Jiorogrear b	ready	,, INDI (IICPAIC	(2011)
	(sulfated, epimer	s, sa	lts: prepara	tion	, epimerization	and sulfation
	of K5 polysacchar					
	of sulfation for					, <u></u>
ΙT	7439-95-4, Magnesiur					processes
	7440-39-3, Barium, p					
	RL: CPS (Chemical pr					
	process): PROC (Proc				_	

(epimerization in presence of; preparation, epimerization and

process); PROC (Process)

sulfation of K5 polysaccharide of Escherichia coli with very high degree of sulfation for cosmetics or pharmaceuticals)

IT 2052-49-5, Tetrabutylammonium hydroxide

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation from Escherichia coli, epimerization and $\underline{\text{sulfation}}$ of K5 polysaccharide with very high $\underline{\text{degree}}$ of $\underline{\text{sulfation}}$

for cosmetics or pharmaceuticals)

IT 42615-44-1P, 5 K (Polysaccharide)

RL: BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(preparation, epimerization and <u>sulfation</u> of K5 polysaccharide of Escherichia coli with very high <u>degree</u> of <u>sulfation</u> for cosmetics or pharmaceuticals)

IT 3402-98-0, Iduronic acid 6556-12-3, Glucuronic acid

RL: BSU (Biological study, unclassified); BIOL (Biological study) (preparation, epimerization and <u>sulfation</u> of K5 polysaccharide of Escherichia coli with very high <u>degree</u> of <u>sulfation</u> for cosmetics or pharmaceuticals)

IT 112567-86-9, D-Glucuronyl C5-epimerase

RL: CAT (Catalyst use); USES (Uses)

(preparation, epimerization and $\underline{\text{sulfation}}$ of K5 polysaccharide of Escherichia coli with very high $\underline{\text{degree}}$ of $\underline{\text{sulfation}}$ for cosmetics or pharmaceuticals)

IT 42615-44-1DP, 5 K (Polysaccharide), sulfated, epimers, salts
RL: COS (Cosmetic use); PRP (Properties); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation, epimerization and $\frac{\text{sulfation}}{\text{degree}}$ of K5 polysaccharide of Escherichia coli with very high $\frac{\text{degree}}{\text{degree}}$ of $\frac{\text{sulfation}}{\text{sulfation}}$

L4 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:117638 CAPLUS

DOCUMENT NUMBER: 138:158842

TITLE: Oversulfated polysaccharides as inhibitors of HIV

INVENTOR(S): Zoppetti, Giorgio; Oreste, Pasqua Anna; Poli, Guido; Vicenzi, Elisa

PATENT ASSIGNEE(S): Fondazione Centro San Raffaele del Monte Tabor, Italy

SOURCE: PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT NO.					KIND		DATE			APPL	ICAT	ION 1	DATE						
 WO	2003	0113	 07		 A1	_	 2003	 0213		 WO 2	 002-		20020726						
	W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	AZ,	BA,	BB,	ВG,	BR,	BY,	BZ,	CA,	CH,	CN,		
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FΙ,	GB,	GD,	GE,	GH,		
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KΖ,	LC,	LK,	LR,		
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,		
		PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ΤJ,	TM,	TN,	TR,	TT,	TZ,		
		UA,	UG,	US,	UZ,	VN,	YU,	ZA,	ZM,	ZW									
	RW:	GH,	GM,	KΕ,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	ΑT,	BE,	BG,		
		CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FΙ,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,		
		PT,	SE,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,		
		ΝE,	SN,	TD,	ΤG														
IT 2001MI1633					A1		2003	0127		IT 2001-MI1633						20010727			

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CA 2454945
                                20030213 CA 2002-2454945
                         A1
                                                                    20020726
                              20030217 AU 2002-319837
20040428 EP 2002-749173
     AU 2002319837
                        A1
                                                                    20020726
    EP 1411956
                        A1
                                                                    20020726
    EP 1411956
                         B1 20050706
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
                             20050707 JP 2003-516537
20050715 AT 2002-749173
20051031 PT 2002-749173
     JP 2005519860 T
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     AT 299027
                                                                    20020726
                        T
    PT 1411956
                                                                   20020726
    ES 2246406
                         T3 20060216 ES 2002-749173
                                                                   20020726
     US 20050009780
                        A1 20050113 US 2004-484883
                                                                    20040818
     US 7268122
                        B2 20070911
                                           IT 2001-MI1633 A 20010727 WO 2002-IB2909 W 20020726
PRIORITY APPLN. INFO.:
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AB The present invention relates to the use of N,O oversulfated K5 derivs. having a $\underline{\text{degree}}$ of $\underline{\text{sulfation}} > 3.2$ or of their

pharmaceutically acceptable salts for the preparation of pharmaceutical compns. for treating the infection and the consequent HIV/AIDS disease. Thus, K5 (polysaccharide) was obtained from E. coli. by a fermentation process, and purified. A N,O-oversulfated K5 was prepared from K5 (polysaccharide), by deacetylation with NaOH solution followed by the N-sulfation and O-oversulfation.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IN Zoppetti, Giorgio; Oreste, Pasqua Anna; Poli, Guido; Vicenzi, Elisa

AB The present invention relates to the use of N,O oversulfated K5 derivs. having a degree of sulfation >3.2 or of their pharmaceutically acceptable salts for the preparation of pharmaceutical compns. for treating the infection and the consequent. . . fermentation process, and purified. A N,O-oversulfated K5 was prepared from K5 (polysaccharide), by deacetylation with NaOH solution followed by the N-sulfation and O-oversulfation.

IT AIDS (disease)

Anti-AIDS agents

Drug delivery systems

Human

Human immunodeficiency virus 1 Molecular weight distribution

Sulfation

(oversulfated polysaccharides as inhibitors of HIV)

L4 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:64061 CAPLUS

DOCUMENT NUMBER: 139:254763

TITLE: Broad spectrum inhibition of HIV-1 infection by

sulfated K5 Escherichia coli polysaccharide

derivatives

AUTHOR(S): Vicenzi, Elisa; Gatti, Alessandra; Ghezzi, Silvia;

Oreste, Pasqua; Zoppetti, Giorgio;

Poli, Guido

CORPORATE SOURCE: AIDS Immunopathogenesis Unit, San Raffaele Scientific

Institute, Milan, Italy

SOURCE: AIDS (London, United Kingdom) (2003), 17(2), 177-181

CODEN: AIDSET; ISSN: 0269-9370

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal LANGUAGE: English

AB HIV-1 entry into CD4 cells represents a main target for developing novel antiretroviral agents and microbicides. Sulfated derivs. of the K5

polysaccharide have a backbone structure resembling the heparin precursor, but are devoid of anticoagulant activity. The derivs, were chemical sulfated in the N position after N-deacetylation, in the O position, or in both sites. HIV replication in human T cell blasts, monocyte-derived macrophages and cell lines was studied in the presence of sulfated K5 derivs. O-sulfated [K5-OS(H)] and N,O-sulfated [K5-N,OS(H)] K5 derivs. with high degree of sulfation inhibited the replication of an HIV strain using CXCR4 as entry co-receptor (X4 virus) in both cell lines and T-cell blasts. K5 derivs. also strongly inhibited the multiplication of CCR5-dependent HIV (R5 virus) in cell lines, T-cell blasts and primary monocyte-derived macrophages. Their 50% inhibitory concentration was between 0.07 and 0.46 μM , without evidence of cytotoxicity even at the maximal concentration tested (9 μ M). In addition, both K5-N,OS(H) and K5-OS(H) potently inhibited the replication of several primary HIV-1 isolates in T-cell blasts, with K5-N,OS(H) being more active than K5-OS(H) on dual tropic R5X4 strains. K5 derivs. inhibited the early steps of virion attachment and/or entry. Because K5 derivs. are unlikely to penetrate into cells they may represent potential topical microbicides for the prevention of sexual HIV-1 transmission.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AU Vicenzi, Elisa; Gatti, Alessandra; Ghezzi, Silvia; Oreste, Pasqua; Zoppetti, Giorgio; Poli, Guido

AB . . . cell lines was studied in the presence of sulfated K5 derivs.

O-sulfated [K5-OS(H)] and N,O-sulfated [K5-N,OS(H)] K5 derivs. with high degree of sulfation inhibited the replication of an HIV strain using CXCR4 as entry co-receptor (X4 virus) in both cell lines and T-cell. . .

L4 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:813944 CAPLUS

DOCUMENT NUMBER: 137:304779

TITLE: Use of sulfated bacterial polysaccharides suitable for

the inhibition of angiogenesis

INVENTOR(S): Zoppetti, Giorgio; Oreste, Pasqua

Anna; Presta, Marco

PATENT ASSIGNEE(S): Universita Degli Studi Di Brescia, Italy

SOURCE: PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PA	PATENT NO.						KIND DATE			APPL	ICAT		DATE				
 WO	2002083155				A1 20021024			,	 WO 2	002-	20020410						
	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	AZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KΖ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
		PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ΤJ,	TM,	TN,	TR,	TT,	TZ,
		UA,	UG,	US,	UZ,	VN,	YU,	ZA,	ZM,	ZW							
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AT,	BE,	CH,
		CY,	DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	ΙΤ,	LU,	MC,	NL,	PT,	SE,	TR,
		BF,	BJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG
ΙT	2001	MI07	79		A1		2002	1014		IT 2	001-1	MI77	9		2	0010	412
AU	AU 2002251412 A1 20021							1028	3 AU 2002-251412						20020410		
PRIORIT	IORITY APPLN. INFO.:								IT 2001-MI779						A 20010412		
									WO 2002-IB1138						W 2	0020	410

AB The present invention refers to the use of N,O-sulfated K5 having a degree of sulfation of at least 2, and of their

pharmaceutical acceptable salts for the preparation of medicaments for treating angiogenesis-dependent diseases.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IN <u>Zoppetti, Giorgio; Oreste, Pasqua Anna; Presta, Marco</u>

AB The present invention refers to the use of N,O-sulfated K5 having a degree of sulfation of at least 2, and of their pharmaceutical acceptable salts for the preparation of medicaments for treating angiogenesis-dependent diseases.

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:676062 CAPLUS

DOCUMENT NUMBER: 137:200359

TITLE: Highly sulfated derivatives of k5 polysaccharide and

their preparation

INVENTOR(S): Zoppetti, Giorgio; Oreste, Pasqua

Anna

PATENT ASSIGNEE(S): Italy

SOURCE: PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

	TENT							APPLICATION NO.										
								WO 2002-IB561										
	W:	ΑE,	AG,	AL,	ΑM,	ΑT,	ΑU,	ΑZ,	ΒA,	ВВ	BG,	BR,	BY,	BZ,	CA,	CH,	CN,	
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC	, EE,	ES,	FΙ,	GB,	GD,	GE,	GH,	
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE	, KG,	ΚP,	KR,	KΖ,	LC,	LK,	LR,	
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN	, MW,	MX,	MZ,	NO,	NΖ,	OM,	PH,	
		PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK	SL,	ΤJ,	TM,	TN,	TR,	TT,	TZ,	
		UA,	UG,	US,	UZ,	VN,	YU,	ZA,	ZM,	ZW	Ī							
	RW:	GH,	GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ	, TZ,	UG,	ZM,	ZW,	ΑT,	BE,	CH,	
		CY,	DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE	, IT,	LU,	MC,	NL,	PT,	SE,	TR,	
		BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ	, GW,	ML,	MR,	NE,	SN,	TD,	ΤG	
CA	2439	337			A1		2002	0906		CA	2002-	2439	337		2	0020	226	
AU	2002	2361	18		A1		2002	0912		AU	2002-	20020226						
AU	2002																	
EP	1366						2003	1203		ΕP	2002-	7025	93		2	0020	226	
EP	1366	082			В1		2006	0104										
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR	i, IT,	LI,	LU,	NL,	SE,	MC,	PT,	
		ΙE,	SI,	LT,	LV,		RO,		•		•							
CN	1529	715			A 20040915					CN	2002-		2	0020	226			
CN	1284	800			С		2006											
JP	2004 3150	5292	27		Τ				JP 2002-567987						20020226			
AT	3150	49			Τ						2002-					0020	226	
	2254										2002-					0020		
	1916										2006-					0020		
	2004									US	2003-	4690	37		2	0030	826	
	6992						2006											
	2005										2004-					0040		
	2008				A1		2008	0619			2007-					0071	-	
PRIORIT	Y APP	LN.	INFO	.:							2001-							
											2002-							
										-	2002-						-	
										US	2003-	4690	37		A3 2	0030	826	

AB The purification of the Escherichia coli K5 polysaccharide by treatment with iso-Pr alc. and elimination of lipophilic substances is described. The purified product can be used to prepare, after N-deacetylation, new N,O-sulfated polysaccharides with high <u>degree</u> of sulfation.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IN Zoppetti, Giorgio; Oreste, Pasqua Anna

AB . . . of lipophilic substances is described. The purified product can be used to prepare, after N-deacetylation, new N,O-sulfated polysaccharides with high degree of sulfation.

ST polysaccharide sulfation

IT Escherichia coli

Sulfation

(highly sulfated derivs. of k5 polysaccharide and their preparation)

L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:817859 CAPLUS

DOCUMENT NUMBER: 136:128792

TITLE: Fibroblast growth factor-2 antagonist activity and

angiostatic capacity of sulfated Escherichia coli K5

polysaccharide derivatives

AUTHOR(S): Leali, Daria; Belleri, Mirella; Urbinati, Chiara;

Coltrini, Daniela; Oreste, Pasqua;

Zoppetti, Giorgio; Ribatti, Domenico; Rusnati,

Marco; Presta, Marco

CORPORATE SOURCE: Unit of General Pathology and Immunology, Department

of Biomedical Sciences and Biotechnology, School of Medicine, University of Brescia, Brescia, 25123, Italy

SOURCE: Journal of Biological Chemistry (2001), 276(41),

37900-37908

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular

Biology

DOCUMENT TYPE: Journal LANGUAGE: English

The angiogenic basic fibroblast growth factor (FGF2) interacts with tyrosine kinase receptors (FGFRs) and heparan sulfate proteoglycans (HSPGs) in endothelial cells. Here, we report the FGF2 antagonist and antiangiogenic activity of novel sulfated derivs. of the Escherichia coli K5 polysaccharide. K5 polysaccharide was chemical sulfated in N- and/or O-position after N-deacetylation. O-Sulfated and N,O-sulfated K5 derivs. with a low degree and a high degree of sulfation compete with heparin for binding to 125I-FGF2 with different potency. Accordingly, they abrogate the formation of the HSPG·FGF2·FGFR ternary complex, as evidenced by their capacity to prevent FGF2-mediated cell-cell attachment of FGFR1-overexpressing HSPG-deficient Chinese hamster ovary (CHO) cells to wild-type CHO cells. They also inhibited 125I-FGF2 binding to FGFR1-overexpressing HSPG-bearing CHO cells and adult bovine aortic endothelial cells. K5 derivs. also inhibited FGF2-mediated cell proliferation in endothelial GM 7373 cells and in human umbilical vein endothelial (HUVE) cells. In all these assays, the N-sulfated K5 derivative and unmodified K5 were poorly effective. Also, highly O-sulfated and ${\tt N,O-sulfated}$ K5 derivs. prevented the sprouting of FGF2-transfected endothelial FGF2-T-MAE cells in fibrin gel and spontaneous angiogenesis in vitro on Matrigel of FGF2-T-MAE and HUVE cells. Finally, the highly N, O-sulfated K5 derivative exerted a potent antiangiogenic activity on the chick embryo chorioallantoic membrane. These data demonstrate the

possibility of generating FGF2 antagonists endowed with antiangiogenic activity by specific chemical <u>sulfation</u> of bacterial K5 polysaccharide. In particular, the highly N,O-sulfated K5 derivative may provide the basis for the design of novel angiostatic compds.

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

- AU Leali, Daria; Belleri, Mirella; Urbinati, Chiara; Coltrini, Daniela;
 Oreste, Pasqua; Zoppetti, Giorgio; Ribatti, Domenico;
 Rusnati, Marco; Presta, Marco
- AB . . . polysaccharide. K5 polysaccharide was chemical sulfated in N-and/or O-position after N-deacetylation. O-Sulfated and N,O-sulfated K5 derivs. with a low degree and a high degree of sulfation compete with heparin for binding to 125I-FGF2 with different potency. Accordingly, they abrogate the formation of the HSPG·FGF2·FGFR ternary complex,. . . chick embryo chorioallantoic membrane. These data demonstrate the possibility of generating FGF2 antagonists endowed with antiangiogenic activity by specific chemical sulfation of bacterial K5 polysaccharide. In particular, the highly N,O-sulfated K5 derivative may provide the basis for the design of novel. . .

L4 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1993:441829 CAPLUS

DOCUMENT NUMBER: 119:41829

ORIGINAL REFERENCE NO.: 119:7459a,7462a

TITLE: Biochemical bases of the interaction of human basic

fibroblast growth factor with glycosaminoglycans. New

insights from trypsin digestion studies

AUTHOR(S): Coltrini, Daniela; Rusnati, Marco; Zoppetti,

Giorgio; Oreste, Pasqua; Isacchi,

Antonella; Caccia, Paolo; Bergonzoni, Laura; Presta,

Marco

CORPORATE SOURCE: Sch. Med., Univ. Bresica, Italy

SOURCE: European Journal of Biochemistry (1993), 214(1), 51-8

CODEN: EJBCAI; ISSN: 0014-2956

DOCUMENT TYPE: Journal LANGUAGE: English

In the present study the authors have attempted a characterization of the biochem. bases of the interaction of human basic fibroblast growth factor (bFGF) with glycosaminoglycans (GAGs) in solution This interaction has been evidenced as the capacity of different GAGs and various sulfated compds. to protect bFGF and different bFGF mutants from tryptic cleavage. Heparin protects bFGF from trypsin digestion in a dose-dependent fashion. Substitution by site-directed mutagenesis of two or more basic residues with neutral glutamine residues in the amino-terminal region bFGF(27-32) or in the carboxyl-terminal region bFGF(118-129) does not significantly affect the protective effect exerted by heparin. In contrast, heparin protection is abolished when the full region bFGF(27-32) is deleted. The capacity of different GAGs to protect bFGF from proteolytic cleavage decreases in the following order: heparin > heparan sulfate > dermatan sulfate = chondroitin sulfates A and C > hyaluronic acid = K5polysaccharide, indicating that both the degree of sulfation and the backbone structure of GAG modulate its interaction with bFGF. This is confirmed by the different capacity of various sulfated compds. (including dextran sulfates, suramin, trypan blue, and sulfate ion) to protect bFGF from tryptic digestion. Moreover, tryptic digestion studies performed with various heparin mols. and dextran sulfates of different size, ranging from 2.0 kDa to 500 kDa, indicate that the number of bFGF mols. which interact with a single mol. of polysaccharide is related to the mol. mass of the GAG and that six hexose residues are

sufficient to protect 1-2 mols. bFGF. In conclusion, the authors findings indicate that the capacity of GAGs to protect bFGF from tryptic cleavage depends upon their size, <u>sulfation</u>, distribution of the anionic sites along the chain, and structural requirements of the bFGF mol. These studies will help to design synthetic oligosaccharides endowed with different bFGF agonist and/or antagonist activities.

AU Coltrini, Daniela; Rusnati, Marco; <u>Zoppetti, Giorgio</u>; <u>Oreste, Pasqua</u>; Isacchi, Antonella; Caccia, Paolo; Bergonzoni, Laura; Presta, Marco

AB . . . sulfate > dermatan sulfate = chondroitin sulfates A and C > hyaluronic acid = K5 polysaccharide, indicating that both the degree of sulfation and the backbone structure of GAG modulate its interaction with bFGF. This is confirmed by the different capacity of various. . . conclusion, the authors findings indicate that the capacity of GAGs to protect bFGF from tryptic cleavage depends upon their size, sulfation, distribution of the anionic sites along the chain, and structural requirements of the bFGF mol. These studies will help to. . .

=> epi near k5 14374 EPI 65 EPIS 14412 EPI (EPI OR EPIS) 637092 NEAR 379 NEARS 637422 NEAR (NEAR OR NEARS) 3112 K5 L5 0 EPI NEAR K5 (EPI(W)NEAR(W)K5) => epik5 2 EPIK5 1.6

=> d 16 1-2 ti

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN

TI Anticoagulant and antithrombotic low-molecular-weight glycosaminoglycans derived from k5 polysaccharide and process for their preparation

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN

 ${\tt TI}$ Epimerized derivatives of K5 polysaccharide with a very high degree of sulfation

=> k5 L7 3112 K5 => 17 and epi 14374 EPI 65 EPIS 14412 EPI (EPI OR EPIS) L8 6 L7 AND EPI

=> d 18 1-6 ti

- L8 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
- TI Inhibition of herpes simplex virus types 1 and 2 in vitro infection by sulfated derivatives of Escherichia coli K5 polysaccharide
- L8 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
- TI Cytokine gene expression and production by human LPS-stimulated mononuclear cells are inhibited by sulfated heparin-like semi-synthetic derivatives
- L8 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
- TI Real-time monitoring of keratin 5 expression during burn re-epithelialization1
- L8 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
- TI Process for the manufacture of N-acyl- (\underline{epi}) $\underline{K5}$ -amine-o-sulfate derivatives and products thus obtained
- L8 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
- TI O-Sulfated bacterial polysaccharides and their use
- L8 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
- TI Kinetic behavior of the long-lived p-anisylcamphenilyl cation in formic acid solutions

=> d 18 1-6 ibib abs

PUBLISHER:

L8 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:1193474 CAPLUS

TITLE: Inhibition of herpes simplex virus types 1 and 2 in

vitro infection by sulfated derivatives of Escherichia

coli K5 polysaccharide

AUTHOR(S): Pinna, Debora; Oreste, Pasqua; Coradin, Tiziana;

Kajaste-Rudnitski, Anna; Ghezzi, Silvia; Zoppetti, Giorgio; Rotola, Antonella; Argnani, Rafaela; Poli,

Guido; Manservigi, Roberto; Vicenzi, Elisa

CORPORATE SOURCE: Viral Pathogens and Biosafety Unit, San Raffaele

Scientific Institute, Milan, Italy

SOURCE: Antimicrobial Agents and Chemotherapy (2008), 52(9),

3078-3084

CODEN: AMACCQ; ISSN: 0066-4804 American Society for Microbiology

DOCUMENT TYPE: Journal LANGUAGE: English

Herpes simplex virus type 1 (HSV-1) and HSV-2 are neurotropic viruses and AΒ common human pathogens causing major public health problems such as genital herpes, a sexually transmitted disease also correlated with increased transmission and replication of human immunodeficiency virus type 1 (HIV-1). Therefore, compds. capable of blocking HIV-1, HSV-1, and HSV-2 transmission represent candidate microbicides with a potential added value over that of mols. acting selectively against either infection. We report here that sulfated derivs. of the Escherichia coli K5 polysaccharide, structurally highly similar to heparin and previously shown to inhibit HIV-1 entry and replication in vitro, also exert suppressive activities against both HSV-1 and HSV-2 infections. In particular, the N,O-sulfated [K5-N,OS(H)] and O-sulfated epimerized [Epi-K5-OS(H)] forms inhibited the infection of Vero cells by HSV-1 and -2, with 50% inhibitory concns. (IC50) between 3 ± 0.05 and 48 ± 27 nM, and were not toxic to the cells at concns. as high as 5 μM . These compds. impaired the early

steps of HSV-1 and HSV-2 virion attachment and entry into host cells and reduced the cell-to-cell spread of HSV-2. Since $\underline{\text{K5}}$ -N,OS(H) and $\underline{\text{Epi}}$ - $\underline{\text{K5}}$ -OS(H) also inhibit HIV-1 infection, they may represent valid candidates for development as topical microbicides preventing sexual transmission of HIV-1, HSV-1, and HSV-2.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:859878 CAPLUS

DOCUMENT NUMBER: 142:54677

TITLE: Cytokine gene expression and production by human

LPS-stimulated mononuclear cells are inhibited by sulfated heparin-like semi-synthetic derivatives

AUTHOR(S): Gori, A. M.; Attanasio, M.; Gazzini, A.; Rossi, L.;

Lucarini, L.; Miletti, S.; Chini, J.; Manoni, M.;

Abbate, R.; Gensini, G. F.

CORPORATE SOURCE: Department of Medical and Surigal Critical Care,

Section of Clinical Medicine and Cardiology,

University of Florence, Florence, Italy

SOURCE: Journal of Thrombosis and Haemostasis (2004), 2(9),

1657-1662

CODEN: JTHOA5; ISSN: 1538-7933

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal LANGUAGE: English

Background: The K5 polysaccharide obtained from Escherichia coli strain O10:K5:H4 is a polymer of the disaccharidic unit formed by D-glucuronic acid and N-acetylglucosamine. This structure is akin to N-acetylheparosan, the precursory polymer of heparin and of heparan sulfate. This structural affinity with N-acetylated heparin and with desulfated heparin makes the K5 polysaccharide extremely useful for the preparation of sulfated heparin-like semi-synthetic derivs. It has been demonstrated that heparins are able to inhibit tissue factor and cytokine production and expression by human monocytes. Objective: The aim of this study was to evaluate the effects of four different heparin-like semi-synthetic derivs. on inflammatory cytokine production and expression by human mononuclear cells. Results: The simultaneous addition of lipopolysaccharide (LPS; 0.2 and 10 μ g mL-1) and the K5 polysaccharide did not inhibit interleukin (IL)- 1β , IL-6 or tumor necrosis factor (TNF)- α production by stimulated mononuclear cells. IL-1 β , IL-6 and TNF- α concns. in supernatants of LPS-stimulated mononuclear cells were not influenced by the addition of N,O-sulfated K5 polysaccharide (KS-N, OS) and epimerized N-sulfated K5 $\overline{\text{polysaccharide}}$ (K5 NS epi) at 5 and 10 μ g mL-1, whereas the addition of epimerized N,O-sulfated K5 polysaccharide (K5-N, OS epi) (5 and 10 μ g mL-1) and O-sulfated $\overline{\text{K5}}$ polysaccharide (K5-OS) (5 and 10 μ g mL-1) to LPS-stimulated cells caused a significant dose-dependent inhibition of IL-1 β , IL-6 and TNF- α . All sulfated heparin-like semi-synthetic derivs. did not influence the IL-10 production by LPS-stimulated mononuclear cells. In LPS-stimulated cells (0.2 and 10 μ g mL-1) K5-OS or K5-N, OS epi at 5 and 10 μ g mL-1 markedly decreased TNF- α mRNA expression. Conclusions: These results indicate that the sulfated heparin-like semi-synthetic derivs. K5-OS and K5-N, OS epi are able to inhibit both expression and production of inflammatory cytokines, whereas they do not influence the anti-inflammatory cytokine IL-10, suggesting a potential role for these products as modulators of inflammatory reactions.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:443522 CAPLUS

DOCUMENT NUMBER: 141:172090

TITLE: Real-time monitoring of keratin 5 expression during

burn re-epithelialization1

AUTHOR(S): Bruen, Kevin J.; Campbell, Chris A.; Schooler, Wesley

G.; de Serres, Suzan; Cairns, Bruce A.; Hultman, C.

Scott; Meyer, Anthony A.; Randell, Scott H.

CORPORATE SOURCE: Department of Surgery, University of North Carolina at

Chapel Hill, Chapel Hill, NC, USA

SOURCE: Journal of Surgical Research (2004), 120(1), 12-20

CODEN: JSGRA2; ISSN: 0022-4804

PUBLISHER: Elsevier Science

DOCUMENT TYPE: Journal LANGUAGE: English

Keratin is a major protein produced during epithelialization following burn injury and is a useful marker for assessing wound healing. Transgenic mice expressing enhanced green fluorescent protein (EGFP) driven by the keratin 5 (K5) promoter (K5GFP mice) were used to monitor keratin expression, and thus, re-epithelialization of burn wounds. K5GFP transgenic mice were created using conventional techniques, with PCR and Southern blot confirmation of transgene incorporation, followed by selection of the line with the most intense and consistent basal epithelial EGFP expression. Epi-fluorescent microscopy of 24 K5GFP mouse flanks and 10 neq. littermate controls was used to characterize EGFP intensity, before wounding and serially for 30 days after administration of a standardized burn wound and excision. Biopsy sections of K5GFP and neg. control mice were stained with K5 antibody and imaged with confocal microscopy to characterize the distribution of EGFP and K5 at baseline and after injury and to examine the correlation between K5 expression and EGFP expression during healing. Green fluorescence intensity increased at the advancing wound margin of burned K5GFP mice, reaching a maximum between days 12 and 15 post-burn and then decreasing as healing completed. K5 and EGFP expression increased in parallel in burned K5GFP mice as demonstrated by confocal microscopy. Thus, EGFP expression correlated with K5 expression during wound healing and therefore serves as a good marker of re-epithelialization. This transgenic model allows noninvasive, real-time assessment of in vivo K5 expression and will be useful in the study of wound healing.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:1007020 CAPLUS

DOCUMENT NUMBER: 140:47542

TITLE: Process for the manufacture of N-acyl-(epi)

 $\underline{\text{K5}}\text{-amine-o-sulfate derivatives}$ and products

thus obtained

INVENTOR(S): Oreste, Pasqua Anna; Zoppetti, Giorgio

PATENT ASSIGNEE(S): Italy

SOURCE: PCT Int. Appl., 74 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

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PATENT NO.
                                                    APPLICATION NO.
                             KIND DATE
                             ____
                                       _____
                                                      _____
      WO 2003106505
                              A1 20031224 WO 2003-IB2339
                                                                                  20030617
      WO 2003106505
                              A9 20040226
           W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
                CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
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                LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
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                FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
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      IT 2002MI1345 A1 20031218 IT 2002-MI1345
                                                                                 20020618
      IT 2002MI1346
                              A1 20031218 IT 2002-MI1346
                                                                                  20020618
      CA 2489866 A1 20031224 CA 2003-2489866
AU 2003240191 A1 20031231 AU 2003-240191
EP 1517924 A1 20050330 EP 2003-732806
                                                                                  20030617
                                                                                  20030617
    R: AT, BE, CH, DE, DK, EG,

IE, SI, LT, LV, FI, RO, MK, CY, AL, IK, EG,

NZ 537216

CN 1675249

A 20050527

NZ 2003-537216

CN 1675249

A 20050928

CN 2003-818933

20030617

MX 2004PA12721

A 20050815

MX 2004-PA12721

IN 2004KN01961

A 20060707

IN 2004-KN1961

ZA 2004010357

A 20050721

ZA 2004-10357

ZA 2004010358

A 20050721

ZA 2004-10358

ZA 2004010359

A 20050721

ZA 2004-10358

ZA 2004010359

A 20050721

ZA 2004-10359

CRITY APPLN. INFO.:

IT 2002-MI1345

A 20020618

IT 2002-MI1854

A 20020827

W 20030617
                                                                                  20030617
PRIORITY APPLN. INFO.:
                                                                             W 20030617
                                                      WO 2003-IB2339
AΒ
      A method is described for the oversulfation of (epi
      )KS-N-sulfates to obtain (epi)K5-amine-O-oversulfates
      at extremely high degree of sulfation and for the transformation of these
      intermediates into new N-acyl-(epi)K5
      -amine-O-oversulfates basically free of activity on the coagulation
      parameters and useful in the cosmetic or pharmaceutical field. Also
      described are pharmaceutical compns. containing, as one of their active
      ingredients, an (\underline{epi}) \underline{K5}-amine-O-oversulfate.
REFERENCE COUNT:
                                    THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS
                                      RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
     ANSWER 5 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
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ACCESSION NUMBER: 2003:991164 CAPLUS

140:23239 DOCUMENT NUMBER:

O-Sulfated bacterial polysaccharides and their use TITLE: Manoni, Marco; Miletti, Sandro; Cipolletti, Giovanni; INVENTOR(S):

Abbate, Rosanna; Gori, Maria Anna

Inalco S.P.A., Italy PATENT ASSIGNEE(S):

U.S. Pat. Appl. Publ., 17 pp., nones SOURCE:

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

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PATENT NO. KIND DATE APPLICATION NO.
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                        A1 20031218 US 2003-347992
     US 20030232785
                                                                   20030121
     US 6900311
                        B2 20050531
    IT 2002MI1294 A1 20031212 IT 2002-MI1294 CA 2489293 A1 20031224 CA 2003-2489293 WO 2003106503 A1 20031224 WO 2003-EP6164
                                                                    20020612
                                                                    20030612
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2003242681 A1 20031231 AU 2003-242681 20030612
EP 1521778 A1 20050413 EP 2003-759939 20030612
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
                                            US 2005-131636 20050517
IT 2002-MI1294 A 20020612
     US 20050234014
                      A1 20051020
PRIORITY APPLN. INFO.:
                                             US 2003-347992 A1 20030121

WO 2003-EP6164 W 20030612
     The present invention refers to the preparation of O-sulfated, N-sulfated or
AΒ
     N-acetylated derivs., both epimerized or non epimerized, of K5,
     K4, and optionally defructosylated K4 and K40 polysaccharides from
     Escherichia coli and to their use as antiinflammatory agents in chronic
     and acute inflammations. These compds., and in particular O-sulfated,
     N-acetylated K5 (K5-OSNAc) and O-sulfated, N-sulfated
     epimerized K5 (K50SNS epi) obtained according to the
     present invention show a specific activity on the main cytokines involved
     in the inflammatory processes inhibiting especially the production of Tumor
necrosis
     factor alpha, interleukin 1 beta and interleukin 6.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
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REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1961:131412 CAPLUS
DOCUMENT NUMBER: 55.131412

DOCUMENT NUMBER: 55:131412
ORIGINAL REFERENCE NO.: 55:24810a-e

TITLE: Kinetic behavior of the long-lived p-anisylcamphenilyl

cation in formic acid solutions

AUTHOR(S): Bartlett, Paul D.; Dills, Charles E.; Richey, Herman

G., Jr.

CORPORATE SOURCE: Harvard Univ.

SOURCE: Journal of the American Chemical Society (1960), 82,

5414-19

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal LANGUAGE: Unavailable

AB Kinetic evidence, together with preparative evidence previously reported (CA 54, 22398h), leads to an interpretation of the behavior of the long-lived p-anisylcamphenilyl cation in formic acid solns. The rate consts. ka, kb, kc, and kd are all too rapid to measure. When p-anisylcamphenilol (I) or p-anisylapocamphene (II) is dissolved in 96.8% formic acid, the fraction F of the material existing as the carbonium ion

(λ maximum 384 m μ , ϵ 51,000) is the sum of two exponentials. Application of an integrated form of eq. 1 allows evaluation of the following rate consts. in sec.-1 at 25° : k1 = 4.78 + 10-3, k2ko/kd = 1.21 + 10-3, k3 = 0.53 + 10-3, k4ko/kd = 0.69 +10-3. k1 is believed to represent the rate constant for a Nametkin rearrangement within the carbonium ion. In 100% formic acid the optical d. of a solution of p-anisylapocamphene reaches a maximum within 2 min. The rate consts. have been approx. evaluated and it appears that the only important difference from 96.8% formic acid is the increase of 0.86 unit in the neg. value of the acidity function HO, which correspondingly increases the value kc/kd. Solns. of p-anisylapocyclene (III), epi-p-anisylcamphenilol, the formates isolated from reaction of I in formic acid for four min. and four hrs., and alcs. obtained from such formates all follow eq. 1. III is equilibrated with the carbonium ion much more slowly than II but is favored at equilibrium relative to II. The rate constant for racemization (-)-II in formic acid, 6 + 10-4, is close to that predicted using values of k5 and k6 estimated from the spectrophotometric kinetic measurements on III, the only sym. compound in the series.

=> d his

L5

(FILE 'HOME' ENTERED AT 09:07:46 ON 24 NOV 2008)

FILE 'CAPLUS' ENTERED AT 09:08:22 ON 24 NOV 2008

E ORESTE PASQUA/AU

L1 46 S E2-E4

E ZOPPETTI GIORGIO/AU

L2 69 S E2-E3

L3 79 L1 OR L2

L4 11 L3 AND DEGREE AND SULFATION

FILE 'STNGUIDE' ENTERED AT 09:09:29 ON 24 NOV 2008

FILE 'CAPLUS' ENTERED AT 09:14:50 ON 24 NOV 2008

0 EPI NEAR K5

L6 2 EPIK5

L7 3112 K5

L8 6 L7 AND EPI